

Prevalence of helicobacter pylori infection and its histopathological correlation in adult celiac patients

Helicobacter pylori infection in adult celiac patients

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Abstract

Aim: Celiac disease (CD) is a chronic autoimmune enteropathy associated with gluten intake in genetically predisposed individuals. Helicobacter pylori (H. pylori) is a common gastric pathogen, and its relationship with CD remains unclear. This study aimed to investigate the prevalence of H. pylori infection and its histopathological effects in adult CD patients.

Material and Methods: This retrospective study includes patients diagnosed with CH at the Gastroenterology Clinic of Fırat University Hospital. Patients with a confirmed diagnosis of CH based on duodenal biopsy were included in the study. H. pylori status was determined by histological evaluation of gastric biopsies taken according to the Sidney protocol. Demographic, clinical, and histopathological data were obtained from patient files.

Results: A total of 216 CH patients were included in the study (174 [80.6%] H. pylori positive, 42 [19.4%] H. pylori negative). There were no significant differences in gender distribution and Marsh classification between the groups ($p > 0.05$). Marsh 3A and 3B (31.6%) were the most common in H. pylori-positive cases, while Marsh 3B (38.1%) was the most common in H. pylori-negative cases. Chronic gastritis was observed at a high rate in both groups (positive 96%; negative 95.2%).

Discussion: Although H. pylori infection is common in patients with Crohn's disease, no significant effect on histopathological findings and Marsh stages has been detected. Our findings indicate that the effect of H. pylori on Crohn's disease remains controversial and therefore requires large-scale, multicenter prospective studies.

Keywords

celiac disease, helicobacter pylori, marsh classification, histopathology

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This study was approved by the Ethics Committee of Fırat University (Date: 2024-08-01, No: 2024/11-05)

Introduction

Celiac disease is a chronic disorder that may develop at any stage of life in genetically predisposed individuals following the consumption of gluten-containing foods. Also referred to as gluten enteropathy, it is an immune-mediated condition characterized by a T-cell-driven immune response to gluten. Affecting approximately 1% of the global population, celiac disease represents a major public health concern due to its relatively high prevalence and potential for serious complications [1-3]. Gluten-containing grains such as wheat, barley, and rye, as well as their derived products, trigger an abnormal immune reaction, resulting in both serological and histopathological alterations. These include the production of tissue transglutaminase, anti-gliadin, and anti-endomysial antibodies, as well as increased intraepithelial lymphocytes in the small intestinal mucosa, crypt hyperplasia, and villous atrophy. The importance of celiac disease has become increasingly recognized in recent decades, with current data indicating a prevalence of approximately 1.4% worldwide and a notable rise in incidence over the past forty years [4,5]. At present, the cornerstone of management remains strict adherence to a gluten-free diet, which is often difficult to sustain in practice and poses considerable social challenges [6]. *Helicobacter pylori* is a bacterium that colonizes the gastric mucosa and plays a well-established role in the pathogenesis of peptic ulcer disease, gastric carcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma [7]. However, its exact contribution to the etiology of dyspepsia, particularly functional dyspepsia, remains uncertain, as many infected patients fail to achieve symptom relief even after successful eradication therapy. This observation suggests the involvement of additional pathogenic mechanisms or host-related factors. Histological evaluation of gastric mucosa obtained through biopsy remains essential for detecting chronic inflammatory changes, atrophy, and other histopathological abnormalities that may not be visible on endoscopic examination alone [8-11]. Genetic and environmental factors are known to play a role in the etiopathogenesis of celiac disease, while comorbid gastrointestinal conditions may also influence its course and clinical presentation. Among these, *Helicobacter pylori* infection can induce mucosal changes that resemble those observed in celiac disease, potentially leading to clinical overlap between the two disorders. The present study aims to investigate the prevalence of *H. pylori* infection in patients with celiac disease and to evaluate its potential clinical impact, as well as possible interactions between the two conditions.

Materials and Methods

The study was approved by the Clinical Research Ethics Committee of Firat University Faculty of Medicine (decision number 2024/11-05, dated 01.08.2024). The research protocol was carried out in accordance with the principles of the Declaration of Helsinki. This retrospective study was conducted at the Adult Gastroenterology Clinic of Firat University Faculty of Medicine Hospital. Patients who had undergone upper gastrointestinal endoscopy for suspected celiac disease prior to 2024 and who demonstrated both positive histological findings and serological test results in duodenal biopsies were included in the study. Biopsy samples obtained from these

patients for *Helicobacter pylori* evaluation, in accordance with the Sydney protocol, were also assessed. Data on patients' sex, age, presenting symptoms, comorbidities, medication use, and biochemical parameters were recorded using standardized clinical data collection forms and retrieved retrospectively from patient files.

Statistical Analysis

Statistical analyses were performed using SPSS v.22 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL). The normality of the distribution of continuous variables was determined using the Kolmogorov-Smirnov test. The Kruskal-Wallis test was used for comparisons between more than two groups. Following the Kruskal-Wallis test, the Post Hoc Dunn test was used for pairwise group comparisons. The chi-square test and Fisher's exact test were performed for categorical data analysis. Numerical data were expressed as Median (IQR), and categorical data as percentage (%). Spearman's correlation test was performed to analyze correlations between continuous variables. Logistic regression analysis was used to calculate risk factors, starting with a univariate analysis, followed by a multivariate analysis for variables found to be significant in the first stage. Statistical significance was set at $p < 0.05$.

Ethical Approval

This study was approved by the Ethics Committee of Firat University (Date: 2024-08-01, No: 2024/11-05).

Results

Among the 216 patients with celiac disease included in the study, 174 (80.6%) were *Helicobacter pylori*-positive, while 42 (19.4%) were *H. pylori*-negative (Figure 1). The gender distribution did not differ significantly between the groups (*H. pylori*-positive: 114 women and 60 men; *H. pylori*-negative: 13 women and 29 men; $p=0.664$).

Histopathological examinations showed that edematous gastric changes were observed in only one *H. pylori*-negative patient (2.4%), a difference that was not statistically significant ($p = 0.116$). Chronic gastritis was detected in 96% of the *H. pylori*-positive group and 95.2% of the negative group. The rates of intestinal metaplasia were 4% and 2.4%, respectively, with no significant difference between the groups.

According to the MARSH classification, stages 3A (31.6%) and 3B (31.6%) were the most common in *H. pylori*-positive patients, while stage 3B (38.1%) predominated in *H. pylori*-negative patients. No statistically significant difference was found in stage distribution ($p = 0.679$).

In terms of clinical symptoms, dyspepsia was present in 81% of *H. pylori*-positive patients and 76.2% of negative patients ($p = 0.480$). Diarrhea was reported in 21.3% of *H. pylori*-positive patients compared with 35.7% of negative patients, a statistically significant difference ($p = 0.049$). Weight loss was observed in 10.3% of *H. pylori*-positive patients and 2.4% of negative patients, although this difference did not reach statistical significance ($p = 0.082$) (Table 1). In the study group, the *Helicobacter pylori* positivity rate was 80.56% and the negativity rate was 19.44% (figure 1).

Discussion

According to our findings, although *Helicobacter pylori* infection is common among patients with celiac disease, it did not have

Table 1. Pathological findings, MARSH classification, and distribution of symptoms in celiac patients according to H. pylori status

	h.pylori positive	HPV negative	p
N (F/M)	174 (114/60)	42 (13/29)	0.664
Pathology			
Edematous stomach, n %	0 (0)	1 (2.4)	0.116
Chronic gastritis, n %	167 (96)	40 (95.2)	
Intestinal metaplasia, n %	7 (4)	1 (2.4)	
MARSH			
2	33 (19)	9 (21.4)	0.679
3A	55 (31.6)	11 (26.2)	
3B	55 (31.6)	16 (38.1)	
3C	25 (14.4)	6 (14.3)	
4	6 (2.8)	0	0.480
Dyspepsia	141 (81)	32 (76.2)	
Diarrhea	37 (21.3)	15 (35.7)	0.049
Weight loss	18 (10.3)	1 (2.4)	0.082

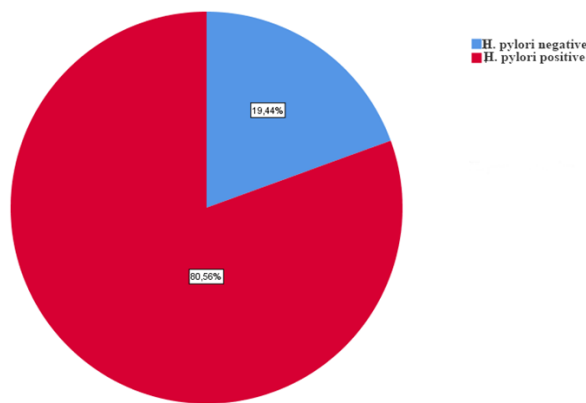


Figure 1. Distribution of helicobacter pylori positivity and negativity in the study population

a significant impact on histopathological findings or MARSH stage distribution. Nonetheless, the higher prevalence of diarrhea observed in H. pylori–negative patients suggests that the bacterium may exert an indirect influence on symptom severity.

The relationship between *Helicobacter pylori* infection and celiac disease has been investigated in numerous studies, yet the findings remain inconsistent [12–14]. For example, a large cross-sectional study by Lebwohl et al. demonstrated an inverse association between H. pylori and celiac disease, even after adjusting for sociodemographic factors, suggesting a possible protective role of the bacterium against celiac disease development [15]. In addition, studies from regions with a high prevalence of H. pylori, such as Latin America, have reported celiac disease prevalence rates comparable to those in European populations, implying that the presence of H. pylori may not be a decisive factor in disease pathogenesis [6,17]. Although H. pylori infection was common in our cohort, no significant association was observed. Taken together with previous evidence, these findings underscore the ongoing controversy regarding the role of H. pylori in celiac disease and highlight the need for larger, well-designed studies to clarify

this relationship.

Histopathological examination remains the gold standard for the diagnosis of celiac disease, gastric lesions, and *Helicobacter pylori* infection [18]. Previous studies have reported that duodenal intraepithelial lymphocytes may increase in patients with H. pylori gastritis and that this finding can be reversed following eradication therapy. Other studies have shown that the clinicopathological features of celiac patients infected with H. pylori do not differ significantly from those without infection, and that both groups demonstrate a similar response to a gluten-free diet. Moreover, it has been suggested that while mild duodenal lesions and lymphocytosis triggered by gastritis are more frequent in H. pylori–infected celiac patients, these changes are associated with lower rates of deep inflammation and stricture compared to other mucosal alterations [19]. Some evidence also indicates that the increase in intraepithelial lymphocytes may, in certain cases, reflect an inappropriate host immune response to H. pylori. Consequently, it has been emphasized that screening for H. pylori infection and considering eradication therapy may be beneficial before initiating a gluten-free diet [20]. Therrien and colleagues reported a prevalence of chronic gastritis of 31.3% among patients with celiac disease [21]. Moreover, their observation of higher antibody titers in cases with gastritis—independent of the degree of villous atrophy—supports the lack of differences in MARSH stages, as the prevalence of chronic gastritis observed in our study was similarly high. In line with this, several studies have suggested that gastric pathologies may influence the duodenum and that *Helicobacter pylori*, after colonizing the gastric mucosa, can contribute to the development of duodenitis. Accordingly, it has been recommended that biopsies be obtained from both the stomach and duodenum in patients presenting with duodenal pathology [22]. Consistent with our results, some studies have also reported that H. pylori infection is less frequent in celiac patients, and that duodenal damage—as assessed by Marsh score—tends to decrease with increasing H. pylori density [13,23]. Villanacci et al. similarly observed milder villous atrophy in H. pylori–positive celiac patients, while another study found a higher prevalence of H. pylori in Marsh grade 1/2 lesions and a lower prevalence in Marsh grade 3 lesions [19,24]. These findings suggest that H. pylori may exert a protective effect by mitigating histopathological damage. However, a multicenter study by Bayrak et al. did not confirm this relationship, reporting no significant association between H. pylori infection and duodenal injury [25].

Limitations

This study has several limitations. First, it was conducted at a single center with a relatively small sample size. Second, due to its cross-sectional design, causal inferences regarding the relationship between *Helicobacter pylori* infection and celiac disease cannot be established, which limits the generalizability of the findings. Third, socioeconomic and environmental factors—both of which are known to influence H. pylori prevalence and celiac disease—could not be evaluated because of the retrospective nature of the study. Fourth, reliance solely on histopathological methods for the diagnosis of H. pylori precluded comparison with alternative diagnostic techniques. Finally, as data on symptom severity were

obtained retrospectively from patient records, the potential for subjectivity and recall bias should be taken into account.

Conclusion

In conclusion, the combined evaluation of our results and previous evidence suggests that *Helicobacter pylori* infection does not exert a decisive influence on histopathological progression in patients with celiac disease. Nevertheless, the potential role of *H. pylori* in modulating symptom severity or attenuating histological damage remains controversial. Further large-scale, prospective studies are warranted to clarify this complex relationship.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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